REMARKS

Introduction

Receipt of a final office action dated May 4, 2007 is acknowledged. In the action, the claims are rejected for obviousness reasons.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Status of the Claims

In this response, claims 1 and 3 are amended and new claim 17 added. Support for the claim amendments can be found throughout the specification, in the originally filed claims, and on page 54, lines 5-14 in particular. Upon entry of this amendment, claims 1-4, 6-9, 13, and 15-17 will be under examination.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

It is acknowledged that the foregoing amendments are submitted after final rejection. But because the amendments do not introduce new matter or raise new issues, and because the amendments either place the application in condition for allowance or at least in better condition for appeal, entry thereof by the Examiner is respectfully requested.

In particular, applicants amended the claims to recite the phrase "lacking 17 or 14 amino acid residues" instead of "lacking 17 or less amino acid residues." The amended claims do not require further searching because the "lacking 14 amino acid residues" would have been encompassed by a search of "lacking 17 or less amino acid residues."

Rejection Under 35 U.S.C. §103

Claims 1, 3, 7-9 and 13 are rejected as allegedly obvious over Goto *et al.*, Blood, 84(6)) (1994) ("Goto"), in view of Hirano *et al.*, US Patent No. 5,914,252 ("Hirano"), and claims 2, 4, 6 and 15-16 are rejected over Goto, in view of Hirano and Kang *et al.*, US Patent No. 5,656,448 ("Kang").

In particular, the Office indicates that Goto describes a solubilized HM1.24 antigen obtained by physically destroying HM1.24 expressing cells in a solubilizing buffer solution and that the solubilized HM1.24 antigen is recognized by an HM1.24 antibody. Additionally, the Office believes that Hirano desribes a sequence of HM1.24 antigen, and that a large amount of the antigen can be obtained by expressing the sequence. Accordingly, the Office concludes that an anti-HM1.24 antibody can be produced and the diagnosis of rheumatoid arthritis can be carried out using the anti-HM1.24 antibody. Applicants respectfully traverse this ground for rejection.

The Supreme Court recently reaffirmed the Graham factors for determining obviousness in *KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S., April 30, 2007). The Graham factors, as outlined by the Supreme Court in *Graham et al. v. John Deere Co. of Kansas City et al.*, 383 U.S. 1 (1966), are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the claimed invention and the prior art; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary consideration. The Supreme Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a), and held that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions. The Court noted that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed, and specifically stated:

> Often, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design

> community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was ***an apparent reason to combine the known elements in the fashion claimed*** by the patent at issue. To facilitate review, this analysis should be made explicit.

KSR Int'l Co. v. Teleflex Inc., slip op. at 14 (emphasis added).

As discussed below, the differences between the prior art and the present application are so substantial, that the cited art cannot render the claimed invention obvious.

Regarding Hirano, even if a full length sequence of the HM1.24 antigen is expressed in a host cell, the expressed HM1.24 antigen is a membrane protein and therefore expressed on the cell surface. And contrary to the Office's assertion, because the membrane protein has low solubility in an aqueous medium, it would be very difficult to isolate and purify a large amount of full length HM1.24 from the cell membrane.

Furthermore, only the present inventors found that if 17 or 14 amino acids are removed from the C terminus of SEQ ID NO: 1 (which already has 48 amino acids deleted from full length HM1.24 of SEQ ID NO: 16), a large amount of soluble HM1.24 antigen can be readily obtained. This specific soluble HM1.24 antigen is recited in the claimed invention and is not described in either Goto or Hirano; the combination of removal of the N-terminal membrane-penetration region AND the C-terminal sequence of 17 or 14 amino acid residues is not previously described.

Moreover, even if one of ordinary skill in the art were inclined to make a soluble HM1.24, the artisan would only remove the membrane penetrating region of full length HM1.24, which is at the N-terminus. The present invention, however, removes not only the N-terminal portion from full length HM1.24 but also the 17 amino acid C-terminal residues as well. In another aspect, the present invention further removes 27 amino acids from the N terminal portion of SEQ ID NO: 1 (SEQ ID NO: 1 already has 48 amino acids deleted from full length HM1.24), and also removes 17 or 14 amino acid C terminal residues as well.

And if only the membrane penetrating region is removed from the full length HM1.24 antigen, about half of the expressed HM1.24 antigen is present in a culture supernatant, and

about half of the expressed HM1.24 antigen is on and bonded to the cell membrane and is therefore insoluble (see, Examples 11, 12 and 13, and figures 8 and 9 of the present application). On the other hand, in the case where both the N-terminal membrane penetration regions and the C-terminal amino acid residues are removed, most of the expressed HM1.24 antigen is present in the supernatant and therefore can be easily isolated and purified (see Example 19 and Figure 13 of the present application).

Thus, a large amount of HM1.24 antigen can be easily produced only if both regions are removed, and only using the inventive soluble HM1.24 antigens of the present invention can an immunochemical assay of an HM1.24 antibody be carried out in a practical procedure.

Furthermore, the deficiencies in Goto and Hirano are not described in Kang. Accordingly, applicants respectfully request the rejection be withdrawn because Goto and Hirano together, or in combination with Kang do not render the present invention obvious.

CONCLUSION

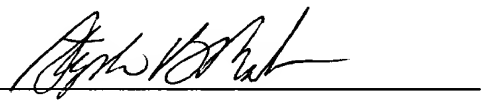
Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

Examiner Davus is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date October 17, 2007

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264